## CLAIMS

1. A method of preparing DNA fragments from a sample of nucleic acids to be analyzed, which method is characterized in that it comprises the selective fragmentation of said nucleic acids by means of at least the following steps:

I. a first selection of short fragments, comprising:

a) the preparation of first double-stranded DNA fragments F1 using at least one restriction enzyme E1 capable of randomly fragmenting the sample of nucleic acids to be analyzed, generating said DNA fragments F1 with blunt or cohesive ends,

b) the ligation of the ends of said DNA fragments F1 obtained in step a) to at least one adapter AA', so as to form a unit - located at the junction of the complementary end of said adapter and of the 5' end of said fragments F1, such that:
- the sequence of said unit is that of the first N-x base pairs of the recognition site - comprising N base pairs - of a restriction enzyme E2, the cleavage site of which is located downstream of said recognition site, with $1 \leq x \leq N-1$, and
- its 3' end - located 5' of said DNA fragments F1 - is that of the restriction site of the E1 restriction enzyme, so as to obtain DNA fragments F'1,

c) the cleavage of the DNA fragments F'1 obtained in b) - in the vicinity of their 5' end - using said restriction enzyme E2, so as to select a fraction of short fragments F2,

d) the purification, by any appropriate means, of said fraction of short fragments F2,
and, optionally,

II. a second selection of one or more subset(s) of fragments from the fraction of short fragments F2 obtained in step d), in accordance with the following steps:

e) the ligation of the free end (not linked to the adapter AA') of short fragments F2 obtained in d) to at least a second complementary adapter BB' (production of fragments F'2), and

f) the amplification of the short fragments F'2 linked to said adapters (AA' and BB'), using at least one pair of appropriate primers, at least one being optionally labeled at its 5' end, so as to select at least one subset of short fragments F'2 from the fraction of short fragments F2 obtained in d).

2. The method as claimed in claim 1, characterized in that step a) is carried out with two different E1 restriction enzymes, $E1_A$ and $E1_C$, such that:
- at least one generates cohesive ends, different from those optionally generated by the other restriction enzyme, and
- the 3' end of the $E1_{1A}$ restriction site is that of the unit as defined in step b).

3. The method as claimed in claim 2, characterized in that one of the enzymes cleaves frequently and the other rarely.

4. The method as claimed in claim 3, characterized in that:
- the enzyme that cleaves frequently is the enzyme $E1_A$, which enzyme $E1_A$ generates at least one end of a fragment F1 that binds to the adapter AA' in step b), and
- the enzyme $E1_C$ that cleaves rarely, generates at least one end of a fragment F1, which binds, in step

b), to a second adapter CC' that is different from the adapter AA'.

5. The method as claimed in any one of claims 1 to 4, characterized in that steps a) and b) are carried out simultaneously.

6. The method as claimed in any one of claims 1 to 5, characterized in that it comprises an additional step consisting of the purification of the fragments less than 1000 bp, prior to the ligation step b).

7. The method as claimed in any one of claims 1 to 6, characterized in that the adapter AA' as defined in step b) comprises, at the 3' end of the strand A and/or 5' end of the strand A', a zone 1 of approximately 1 to 8 bases or base pairs, which is partially or completely identical or complementary to the restriction site of the enzyme E1, which zone 1 is chosen so as to reconstitute the sequence of the first N-x bases or base pairs of the recognition site of the restriction enzyme E2, by ligation of said adapter AA' to the ends of said DNA fragments obtained in a).

8. The method as claimed in claim 7, characterized in that said zone 1 includes one or more mismatches with the sequence of said cleavage site of the restriction enzyme E1.

9. The method as claimed in any one of claims 1 to 8, characterized in that the adapter as defined in step b) comprises, upstream of the zone 1, a zone 2 of at least 6 base pairs.

10. The method as claimed in any one of claims 1 to 9, characterized in that the adapter as defined in step b) comprises at least one base located between the zone 1 and the zone 2, different from that which, in the cleavage site of the restriction enzyme E1, is

immediately adjacent to the complementary sequence corresponding to the zone 1.

11. The method as claimed in any one of claims 1 to 10, characterized in that the adapter as defined in step b) comprises a phosphate residue covalently linked to the 5′ end of the strand A′.

12. The method as claimed in any one of claims 1 to 11, characterized in that, when said method consists of a single selection of short fragments according to steps a) to d), it comprises at least one additional step b′), c′) and/or d′) consisting of the amplification of the fragments F′1 or F2 using an appropriate pair of primers, preferably a pair of labeled primers.

13. The method as claimed in any one of claims 1 to 12, characterized in that the adapter AA′ as defined in step b) is linked, at the 5′ end of its strand A, to an appropriate label, in particular a label for detecting nucleic acid hybrids or a label that can attach to a functionalized solid support.

14. The method as claimed in any one of claims 2 to 13, characterized in that the 5′ end of the strand C′ of the adapter CC′ is linked to a label, which label can attach to a functionalized solid support.

15. The method as claimed in any one of claims 12 to 14, characterized in that the fragments F′1 obtained in step b) or b′) are brought into contact with said functionalized support prior to the cleavage step c), and the fraction of short fragments F2 of step d) corresponds to the fraction of fragments that is either retained on said support (adapter AA′ linked to the label that attaches to the support) or free (adapter CC′ linked to the label that attaches to the support).

16. The method as claimed in any one of claims 1 to 11 and 13 to 15, characterized in that it comprises, in step e), the ligation of several different complementary adapters ($B_1B_1'$, $B_2B_2'$, etc.), each comprising, at the 5' end of the strand B or at the 3' end of the strand B', a specific sequence of 1 to 10 bases.

17. The method as claimed in any one of claims 1 to 11 and 13 to 16, characterized in that said adapter BB' as defined in step e) comprises a phosphate residue covalently linked to the 5' end of the strand B.

18. The method as claimed in any one of claims 1 to 11 and 13 to 17, characterized in that one of the primers as defined in step f) is linked, at its 5' end, to an appropriate label.

19. The method as claimed in any one of claims 1 to 18, characterized in that it comprises an additional step d") or g) consisting of the obtaining, by any appropriate means, of single-stranded fragments from the short fragments F2 obtained in step d) or d') or else from the short fragments F'2 obtained in step f).

20. The method as claimed in any one of claims 1 to 19, characterized in that it comprises an additional step consisting of the purification, by any appropriate means, of the amplification products obtained in step b'), c'), d') or f) or of the single-stranded fragments obtained in step d") or g).

21. A short DNA fragment, representing a genetic marker, that can be obtained by means of the method as claimed in any one of claims 1 to 20, characterized in that it has a sequence of less than 100 bases or base pairs, comprising at least one specific sequence consisting of a fragment of genomic sequence or of cDNA sequence bordered, respectively, by the recognition

site and the cleavage site of a restriction enzyme E2, the cleavage site of which is located downstream of said recognition site, such that the 5' end of said specific sequence corresponds to the last x base pairs of the recognition site - having N base pairs - of said enzyme E2, with $1 \leq x \leq N-1$, said marker including, at each end, at least 6 bases or 6 base pairs of nonspecific sequence.

22. The DNA fragment as claimed in claim 21, characterized in that it is a single-stranded fragment.

23. The DNA fragment as claimed in claim 21 or claim 22, characterized in that it is linked, at one of its 5' ends, to an appropriate label.

24. A DNA chip, characterized in that it comprises a DNA fragment as claimed in any one of claims 21 to 23.

25. The use of a DNA fragment as claimed in any one of claims 21 to 23, as a genetic marker.

26. The use of a mixture of DNA fragments as defined in step d) or f) of the method as claimed in any one of claims 1 to 20, in step d') of the method as claimed in claim 12, or in step d") or g) of the method as claimed in claim 19, as a genetic marker.

27. A method of hybridizing nucleic acids, characterized in that it uses a DNA fragment as claimed in any one of claims 21 to 23 or a DNA chip as claimed in claim 24.

28. A kit for carrying out a method of hybridization, characterized in that it comprises at least one DNA fragment as claimed in any one of claims 21 to 23 or a DNA chip as claimed in claim 24.

29. The kit as claimed in claim 28, characterized in

that it also comprises an oligonucleotide probe complementary to said DNA fragment.

30. The use of an adapter AA' as defined in any one of claims 7 to 11, in combination with a restriction enzyme E2 as defined in claim 1, for preparing genetic markers as defined in any one of claims 21 to 23.

31. A kit for carrying out the method as claimed in any one of claims 1 to 20, characterized in that it comprises at least one adapter AA' as defined in any one of claims 7 to 11, and a restriction enzyme E2 as defined in claim 1.

32. The kit as claimed in claim 31, characterized in that it also comprises at least one adapter BB' as defined in claim 1, 16 or 17, and a pair of primers as defined in claim 1 or 18.